PART B - CHAPTER 2

STUDY DESIGN

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GUIDELINE 875.2000

2.1 INTRODUCTION

The Agency requires that, when certain toxicity and exposure criteria have been triggered (as delineated at 40 CFR 158.390), postapplication monitoring data be submitted. These data may include human exposure and chemical dissipation data (e.g., dislodgeable foliar and transferable residues). The first step in undertaking any postapplication monitoring study is to develop a study design. The Agency requires investigators to submit draft study protocols for review prior to initiating work on a study. Along with the other components of the study design described in this Guideline, these draft protocols should include contingency plans for major weather events, attrition of study participants, or other circumstances that may adversely affect successful completion of the study. All protocols must also be developed in accordance with the requirements stipulated in 40 CFR 160: *FIFRA Good Laboratory Practices* (U.S. EPA, 1989). They should also provide a comprehensive rationale for the choice of sites and activities to be monitored as well as other aspects of the study (e.g., crop selection, season of activity). Agency review of draft protocols is **required** to provide registrants with clarification concerning the scope of each study. Additionally, protocol review by the Agency prevents misinterpretation of the study during regulatory action based on the data generated in the study.

This Guideline provides an overview of the key study design considerations required to conduct studies under Series 875, Group B. Section 2.2 - Experimental Design addresses factors such as the selection of sites and activities to monitor, and issues associated with geographic and seasonal variability. Section 2.3 - Number of Samples and Replicates addresses the numbers of human exposure and environmental data points required for study completion. Section 2.4 - Test Safety describes the requirements for protecting human test subjects involved in research activities. Section 2.5 - Materials and Methods includes information concerning selection of the test material, pesticide application processes, and monitoring techniques for determining both human exposure and environmental concentrations. Section 2.6 - Sample Handling and Collection Procedures addresses general requirements associated with handling and collecting samples and Section 2.7 - Analytical Chemistry provides general guidance on the types of information that should be included in the study design protocol on the analytical chemistry methods used. Study design requirements for ensuring the quality and reliability of the data are described in Section 2.8 - Quality Assurance and Quality Control. This guideline also describes critical elements of Good Laboratory Practices (40 CFR 160) that should be considered during the study design phase. Additionally, contingency planning and reporting and record keeping issues are described in Sections 2.2 and 2.10. The discussion in this Guideline is limited

to the design of studies aimed at gathering postapplication exposure and chemical dissipation data. Sampling techniques, monitoring methods, and other data requirements are described in Part B, Chapters 3 through 12. Details on fulfilling quality assurance and quality control needs are described in Part C. The toxicity data used in the calculations are from data generated under 40 CFR 158.340 requirements. Guidance for calculations based on the resulting data are provided in Part D.

2.2 SITE SELECTION CONSIDERATIONS

The first step on designing a postapplication exposure monitoring or chemical dissipation study is to consider the following five questions:

- Which use patterns and activities should be monitored?
- Which geographical and climatological regions should be monitored?
- What sites should be monitored?
- In what seasons should monitoring occur?
- What use patterns reflect critical market share?

Generally, investigators should choose a combination of sites, activities, and geographical/climatological regions that represent the use of a pesticide product and that will be reflective of the toxicological endpoint of concern. For example, for a compound with a dermal toxicity endpoint, postapplication monitoring should be conducted for activities that could result in dermal exposure. Agency assessments are based on endpoints specified in *Toxicology Endpoint Selection Documents* by the Health Effects Division of the Office of Pesticide Products under *Subdivision F: Toxicology, Human and Domestic Animals* (40 CFR 158). Investigators are required to submit protocols prior to the initiation of any study in order to provide the Agency with a chance to review the design and to provide comments to ensure that the data generated will be appropriate to address the questions concerning the safety of the pesticide product in question.

Pesticide active ingredients may be registered to control a wide variety of target pests in agricultural, industrial/commercial, and residential settings (e.g., a household insecticide may also be registered to control leaf miners in tomatoes and as a fly control agent in a food processing facility). When designing a study, investigators must decide which uses should be monitored and which uses can be considered representative of several pesticide product uses in the risk assessment process. This is necessary because, for many chemicals, it is not feasible to generate data for every possible exposure scenario. The Agency recommends that such decisions be made based on a strategy that considers application rates and frequency, potential for exposure, geographic and climatic regions, and market share. Investigators are encouraged to utilize the guidance provided in Figure B2-1 and in Sections 2.2.1 through 2.2.5 in the site selection phase. A decision logic is

presented in Figure B2-1 that addresses each of these critical issues. This guidance may also be used to assist investigators with the development of an overall strategy for completing studies in support of their products. Chester (1993) and Fenske and Teschke (1995) also provide guidance pertaining to the design and conduct of pesticide exposure studies.

2.2.1 Use Patterns and Activities

During agricultural reentry, a worker may perform various tasks such as thinning, crop harvesting, and canopy management. Commercial/industrial reentry activities can include work with treated oil drilling muds, entry into fumigated shipping containers, and contact with sanitized surfaces in a health care facility. Residential reentry activities of concern include children playing on treated lawns, inhalation exposure resulting from a termiticide application, and nondietary ingestion of chemical residues due to mouthing an object contaminated with pesticide residues. In the study design, investigators need to specify which activities will be monitored during the study (e.g., pruning, picking, playing, etc.). Investigators should also provide justification for why those activities were selected.

The following factors should be considered in deciding which activities/use patterns to monitor:

- Magnitude of Exposure. For some long-term effects (i.e., carcinogenicity), the study investigator may decide to monitor activities that would result in typical exposure (i.e., provide data on the central tendency). Conversely, for short-term acute effects the investigator may monitor activities that would result in worst-case exposures (i.e., high-end) . Investigators should not select sites that will minimize the potential for exposure based on some obvious factor such as mechanical vs. hand harvesting of the same crop.

- Representativeness. The chosen activity should be representative. Representativeness should be based on whether the monitored activities are reflective of the activity of interest or whether the use pattern is typical for the pesticide product. For example, in indoor scenarios such as residential exposure after a termiticide treatment, investigators should consider construction type and ventilation patterns. Data generated from a house with a basement in Maryland may not serve as an adequate surrogate for a typical slab house in Florida because of construction type and the regional use pattern. In addition, sampling should be done in the zone of contact to ensure that sample results are representative of human exposures. For example, sampling should occur in those parts of the crop where workers conduct their activities (i.e., it may not be necessary to sample on the border of a crop where there is little contact). Investigators must also be careful not to alter typical behavior patterns of test subjects during any study (e.g., sampling techniques must be as unobtrusive as possible). If the monitoring technique, regardless of which is selected, interferes with the behavior of the test subject,

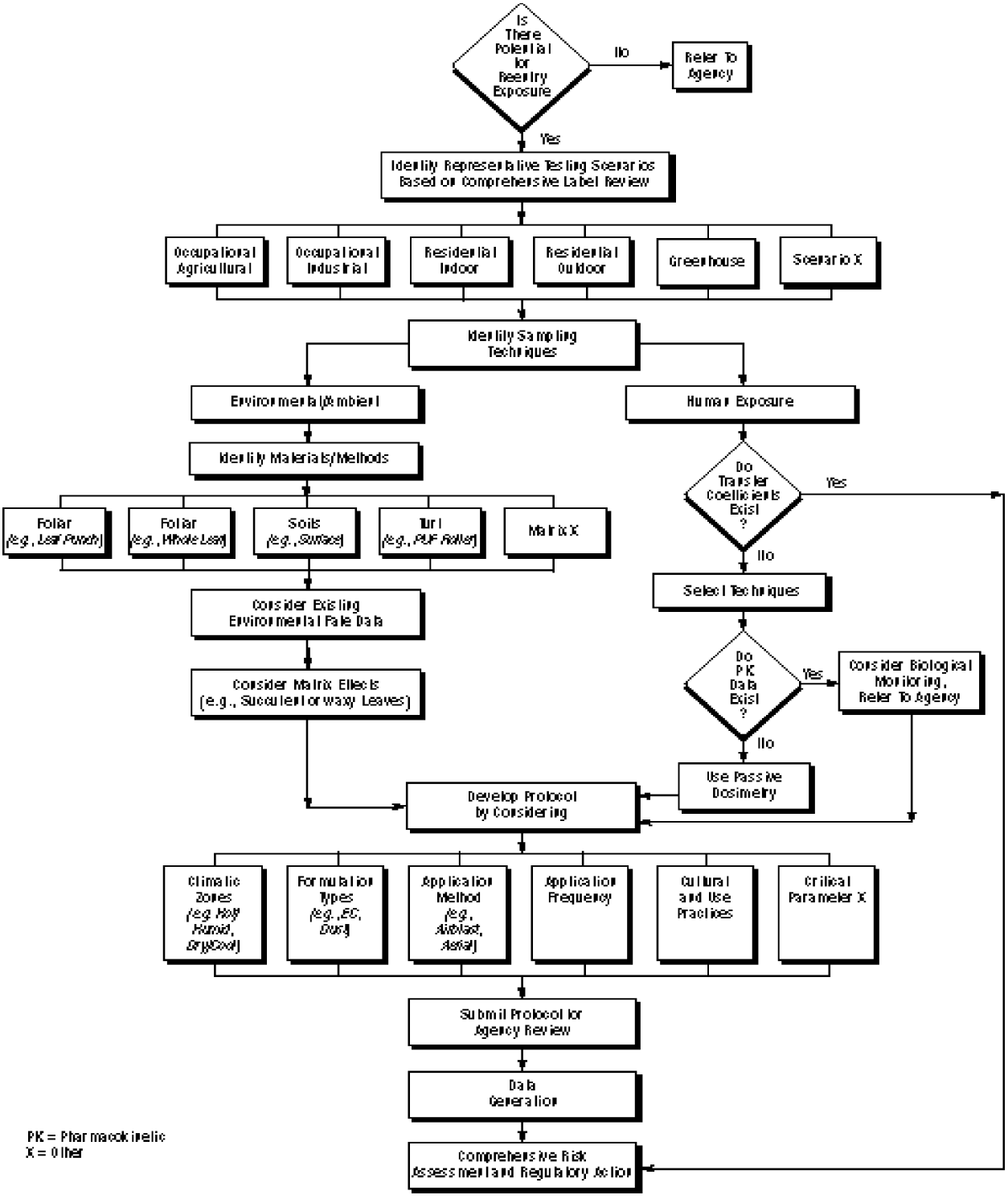


Figure B2-1. Decision Tree for Site/Activity Selection

investigators must describe the effects and how the monitored exposure levels may be impacted.

- Cultural and Use Practices. Cultural practices can vary within regions for particular sites. As a result, variability in cultural practices should be considered. For example, orchard fruit harvesting may be completed using ladders and baskets or with mobile power equipment (i.e., cherry pickers). Additionally, practices may vary in commercial/industrial uses. For example, varying types of ventilation practices exist in facilities where antimicrobial pesticides are added to industrial processes and products.

2.2.2 Geographic and Climatological Considerations

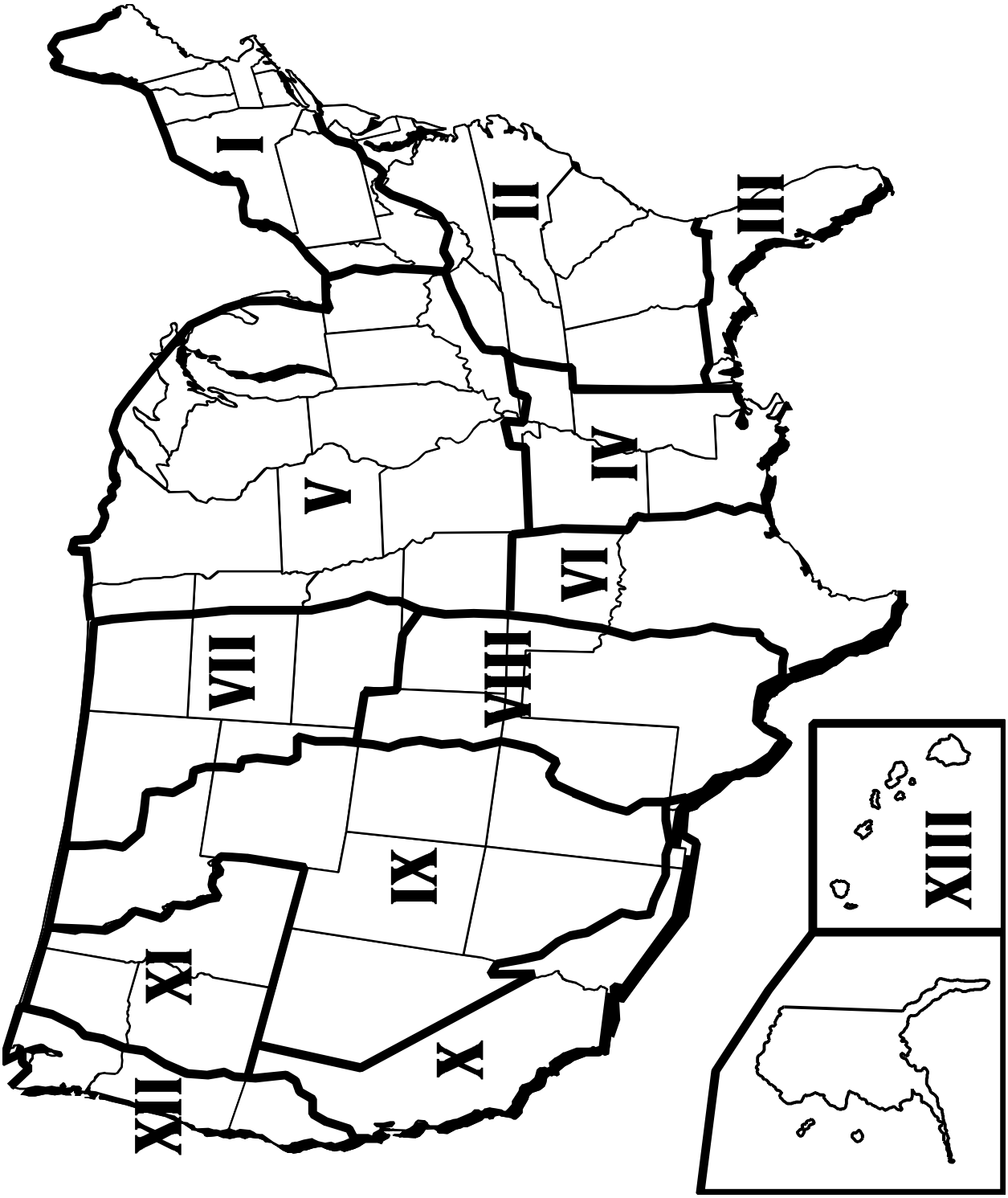
A monitoring study must take place in a location and climate similar to that of the use pattern of interest. Factors to consider in identifying geographical and climatic regions for outdoor monitoring studies (e.g., agricultural reentry or lawn/turf residential exposure) include the following:

- Representativeness. Data must be collected in those geographic regions where the chemical is used (e.g., almonds are grown almost exclusively in California). The Agency has developed a map that delineates regions for completing studies under *Subdivision O: Residue Chemistry*. The map divides the United States into 13 distinct regions. (See Figure B2-2.) Investigators should consider these regions when defining the types and numbers of studies that are to be completed in support of a pesticide active ingredient (i.e., the defined regions may assist investigators in defining chemical use regions).

- Climate. The study must be conducted in a climate that is typical for the pattern of interest. Investigators are encouraged to consult National Weather Service data to determine if climatic differences exist between regions for the pesticide of interest. Contingency plans for catastrophic or atypical weather events must also be considered in the design of the study (e.g., fluke rainstorm in arid California region during a foliar dislodgeable residue study). Refer to Part C, QA/QC -- for detailed information on acceptability criteria for providing climatological data.

- Miscellaneous. Several environmental factors, such as soil types, cultural practices, and pest populations, may vary among regions. Significant variations among cultural practices can occur as a result of these factors. Study investigators should consider regional practices and label requirements when developing study designs.

In the study design, the source and type of weather data to be collected must be specified. Minimally, data on air temperature, humidity, and rainfall during the monitoring period must be collected. Other data such as wind speed/direction and soil temperature should also be considered as


I
II
III
IV
V
VI
VII
VIII
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X
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XII
XIII

Figure B2-2. Residue Chemistry Trial National Regions

appropriate. Surrogate data from a nearby site may be acceptable, but discretion in the use of such data is advised. On-site monitoring of rainfall is highly recommended.

For indoor sites, the following should also be considered:

- Geographic Variation. Use patterns, construction techniques, and other factors that may affect indoor postapplication exposure to pesticides on a regional basis must be considered. Termiticide use in the Northeast versus Florida is an appropriate example. Generally, construction types vary within regions. Basements are not common in Florida due to the water table, but they are common in the Northeast. Termiticide application techniques vary due to construction types. Varying techniques may impact inhalation exposure levels.

- Climatic Variation. Indoor monitoring may be impacted by climatic variation as these variations may affect both construction types and human behavior patterns. Generally, residences are less insulated in warmer climates. Hence, air exchange rates for those types of buildings are generally higher (i.e., more dilution of indoor air contaminants is likely). Additionally, air conditioning (HVAC) systems may be used more frequently in warmer climates.

2.2.3 Sites/Populations to Monitor Within a Region

Once investigators have identified which activities/use patterns and geographic/climatic regions are appropriate, a specific site/population must be identified within a selected region for monitoring purposes. Generally, these sites must represent a "worst case" potential for exposure unless investigators can otherwise justify the use of a different scenario.

In choosing outdoor sites, the investigator must consider four factors:

- Crop Canopy/Maturity. For candidate agricultural sites within a geographic/climatic region, investigators should consider the level of the crop canopy and general maturity of the crop as it relates to typical reentry activities. This is critical as it is believed that dermal exposure levels may be directly related to the extent of contact with foliage and the maturity of the foliage (i.e., dermal exposure during agricultural reentry is generally the predominant exposure route). Investigators should be careful to select residential sites that are typical of the turf in the region (e.g., common grass variety, numbers of pesticide applications, fertilizers, etc.).

- Cultural Practices. For candidate sites within a geographic region, investigators should consider cultural practices. Cultural practices may include grape canopy management, tree trimming/propping, turf mowing, and grape girdling. The impact of variations in cultural practices within regions is difficult to quantify. However, it is likely that such variability can impact exposure levels for a given reentry activity (e.g., grape trellising and girdling

practices between growers in California may vary enough to impact exposure levels within the region).

- Populations. Within geographic regions there are often occupational populations that complete various reentry activities. Investigators should consider the levels of experience within a subject population in the design of the study. The individuals chosen for the study should be representative of the exposed population. Ideally, the test population should be involved in the type of work on a regular basis and be familiar with the activities and purpose of the study. For example, test subjects should be normal workers and not inexperienced volunteers. Likewise, for residential studies, the test populations should be representative of the exposed homeowners/residents population.

- Representativeness. Within a region, representativeness depends upon the crop canopy, the associated cultural practices, and the populations who are subject to human exposure monitoring. Investigators should be careful to assess each of these issues within a region that has been selected for a study. Investigators should provide in any submission to the Agency a rationale detailing the general and specific aspects of the site selection process.

When choosing indoor sites, investigators must consider two additional factors:

- Construction Type. Pesticides can be applied in residential, commercial, and industrial indoor settings. Construction type may impact the distribution and longevity of chemical residues within treated buildings because of the differences in air exchange rates, insulation levels, hard surface types, and the general use of common construction materials. Investigators should consider these parameters in the study design process. For example, if postapplication inhalation exposure after a termiticide application is to be monitored, investigators should address the four basic residential construction types (i.e., slab, basement, crawl space, and plenum) in their protocols.

- Ventilation Procedures. One of the key concerns for the Agency is addressing postapplication inhalation exposure after indoor treatments of a pesticide. Along with construction type, the air exchange rate is probably the most critical parameter that affects airborne concentrations over time. Therefore, air exchange rates must be considered by investigators in the design of their studies. Generally, investigators should describe the use of any ventilation (i.e., HVAC and/or natural) over the course of a study and should describe the dimensions/layout of any building under study.

2.2.4 Time of the Year for Monitoring

Studies should be conducted during the season(s) when exposure is of most concern and where conditions pose the greatest risk for human exposure. For any postapplication monitoring, data must be collected during the season that the particular exposure scenario normally occurs (e.g., agricultural reentry during a typical harvest season, indoor residential air during common pest seasons, etc.).

2.2.5 Market Share

In developing a strategy to support labeling for an active ingredient, investigators should consider all uses that are allowable by current or proposed labeling as well as the core market for their product. Market share analysis can assist investigators in the development of a strategic plan for selecting and designing their studies (e.g., typical and unusual application rates, seasons, crops, etc.). Investigators should consider the possible confidential nature of this type of information if they are to be included in a study protocol.

2.3 NUMBER OF SAMPLES AND REPLICATES

The numbers of datapoints generally required under Series 875, Group B are presented below for human exposure monitoring and the characterization of chemical dissipation in the environment as well as in residential, commercial, and industrial settings. Both the number of sites required for each type of monitoring and the number of replicate datapoints at each site are described. The number of samples and replicates presented below are general guidance. Investigators are required to submit protocols prior to initiating any study to ensure that an adequate dataset is generated.

Chemical Dissipation. A dissipation study involves taking a number of samples over a period of time to characterize the rate of dissipation of a pesticide. Such a study would start on the day of pesticide application. (See Part B, Chapters 3, 4, 5, and 6 for further description of the sample collection methods.)

- Geographic Location. The study investigator should carry-out dissipation studies at a number of locations. Generally, samples are collected at a minimum of three sites. Sampling at multiple sites is usually necessary to ensure that the varying climatic conditions, crops, and pest types are represented. The location and number of sites selected for use in a study must be justified by investigators to the Agency. Investigators will need to justify site selection based on the criteria described above (e.g., on the nature of the use scenario and the number of regions where the target crop is grown or structural pests are located).

- Sampling Period and Intervals. The dissipation study should be carried out over a long enough period to characterize the dissipation rate of the pesticide under investigation. Generally, the first sampling intervals will be just before and after application (i.e., t=0). Subsequent samples should be collected (that are appropriate for the pesticide under investigation) at periodic intervals over the course of the study. During each sampling interval, a minimum of 3 replicate samples need to be collected at each treated study site.

Human Exposure Study. A human exposure study involves determining the amount of pesticide exposure that occurs during a given activity. (See Part B, Chapters 7, 8, and 10 for further description of these requirements.)

- Number of Subjects to Monitor. Generally, a minimum of 15 monitoring replicates need to be completed for each reentry activity of concern. Investigators should attempt to obtain data from as many test subjects as inter-test subject differences are a primary source of variability. The statistical robustness of the data set will increase with increased number of replicates.

- When to Monitor. Generally, exposure replicates should be completed based on the following distribution: 5 replicates/day on each of 3 days after the application of the pesticide product. Monitoring should be conducted before residues have dissipated beyond the limit of quantification.

2.4 TEST SAFETY

In the study design, it should be indicated what clothing will be worn by the subjects in the study. For example, will normal work clothes be worn, and will any form of personal protective equipment be used? The type of personal protective equipment recommended for the pesticide of interest should be considered during the study design phase. Regulations that must be considered in making the decisions about protection of study participants include those of the country where the study is being conducted. For example, in the United States, these regulations include the Worker Protection Standard and Informed Consent. These are described below.

The Worker Protection Standard. In conducting any field study, the investigator must insure that the applicable provisions of the Worker Protection Standard regulations are being fulfilled. Generally, hazard information must be available for all workers, appropriate protective clothing must be provided, and decontamination sites and emergency assistance must be available. To determine what you must do to comply with the Worker Protection Standards, refer to the Code of Federal Regulations (40 CFR Part 170) and/or contact the Certification and Worker Protection Branch, Office of Pesticide Programs, U.S. EPA at (703) 305-7666.

Informed Consent. Investigations carried out under these guidelines must be properly designed to provide for maximum protection of the study subject's health. Studies conducted to obtain human exposure data must not violate Section 12(a)2(P) of FIFRA. Specifically, informed consent should be obtained in writing from all subjects who will be exposed as a result of these studies. Also, proposed protocols may need to be approved by the appropriate human studies committee for the state in which the exposure will occur. Investigators are also encouraged to review the requirements of the *Federal Policy for the Protection of Human Subjects; Notices and Rules* otherwise referred to as the "Common Rule" (U.S. EPA, 1991).

2.5 MATERIALS AND METHODS

This section includes a general description of the study design considerations for selecting an end-use-product test material, defining an application method, and developing a monitoring strategy. Selection of a proper test material is dependent upon the labeling for each end-use-product, and the physical-chemical properties of the pesticide active ingredient in the product. Selection of a proper application method should be reflective of the exposure scenario to be monitored. Additionally, techniques used to monitor human exposure and environmental dissipation should be durable and provide appropriate data (e.g., biological monitoring would not be used for a chemical with no pharmacokinetic data). Monitoring techniques are described in Part B, Chapters 3 through 8 and in Chapter 10 of this document. Refer to these chapters for specific information regarding the technology and methods recommended by the Agency for developing field monitoring data. The Agency encourages the use of novel or alternative technologies for generating data to satisfy these guidelines. However, if investigators opt to develop data using such an approach, a justification for the approach must be prepared and submitted to the Agency as part of the study protocol for review purposes prior to the initiation of any such study.

2.5.1 Test Material

Typically, active ingredients are marketed in several formulations. As such, investigators must select which formulations will be used as test materials in any study to support their product. Representative end-use product formulations (e.g., wettable powder, emulsifiable concentrate) must be used to make all treatment(s) to the site under investigation. Significant differences in residue dissipation rates and exposure levels are thought to exist among different end-use products containing the same active ingredient (e.g., the wettable powder formulation of a given pesticide may be more persistent than the emulsifiable concentrate). Therefore, the end-use product to be applied must be the formulation type that is most likely to be persistent and/or that inherently poses the highest risk in terms of exposure during reentry operations. The study design must include a description of the formulation to be used in the study, and a rationale for selecting the formulation.

2.5.2 Pesticide Application

The method of application (groundboom spray, airblast spray, broadcast granular, etc.) should be specified, and the type of equipment to be used should be indicated. Generally, the pesticide should be applied so that the greatest exposure potential is achieved (i.e., highest allowable rates with minimum intervals between applications). However, if the pesticide under consideration is known to be a carcinogen,

then typical application rates may be more appropriate. The pesticide must be applied under conditions that are consistent with the label requirements of the formulated end-use product.

2.5.3 Description of Methods For Monitoring Pesticide Concentration

The study design should provide a description of which methods will be used to measure each of the analytes under investigation (e.g., PUF roller, hand washes for dermal, etc.) in each of the matrices (e.g., air, soil, foliar) of concern. For inhalation exposure, the technique (pump/absorbers, impingers, etc.), sampling media (e.g., nature of sorbent in absorbers, liquids in impingers), types of pumps, positioning and flow rates, if appropriate, must be specified. For dermal exposure, the method for measuring hand exposure (gloves, hand rinse, etc.) must be specifically described, as well as the types of dosimeters to be used for evaluation of the other parts of the body. If the patch method is to be used for dermal exposure evaluation, the number and locations of the patches must be indicated, including whether patches are to be placed inside or outside normal clothing, or both. If biomonitoring is to be employed, the procedures and rationale should be described in detail.

Critical factors that may need to be addressed in the selection of monitoring methods include:

- The environmental fate and/or transport characteristics of the active ingredient;
- Major pathways through which the pesticide may degrade or dissipate; and
- The durability of dosimeters and sample collection devices; they must be designed to: (1) survive the duration of the monitoring effort; (2) be the most appropriate for the pesticide; (3) avoid overloading during the collection period; and (4) survive storage and shipment to the analytical laboratory and not have losses of residues due to the storage containers (e.g., leaching of residues into matrix of plastic bag).
- The need to change clothing, gloves, or samples, or wash hands during the workshift in case of breakthrough or to coincide with natural breaks in the day.

2.6 SAMPLE HANDLING AND COLLECTION PROCEDURES

Defining sample collection procedures prior to initiating the field phase of any study ensures added integrity for the samples. It also lowers the risk to the investigators of study failure due to unforeseen analytical problems. The study design should provide a description of:

- The preparation of sampling devices prior to the conduct of the study;

- The sample collection procedures to be employed;
- The methods and precautions to be used in removing samplers from workers; and
- Storage and shipment procedures to be employed.
- Select sample storage vessels that allow for quantitative transfer of residues into an extraction vessel or that serve as the extraction vessel itself.

2.7 ANALYTICAL CHEMISTRY

In the study design the study investigator should briefly describe which analytical methods will be used to measure the analyte(s) of concern. Also, the study investigator should indicate (if known) the stability of the analyte and describe how the stability of each analyte under investigation will be verified. Finally, in the study design the study investigator should indicate the proposed limits of quantitation for each analyte. Described in Part C are specific analytical routines for characterizing the stability of the analyte and more information on providing and determining the limits of quantitation.

2.8 QUALITY ASSURANCE AND QUALITY CONTROL

The data collected in a study should be of sufficient quality and quantity to support defensible decisionmaking, especially for critical measurements needed to meet project objectives. In designing any study, QA/QC measures must be built into the study early in the process. Inherent to the QA/QC process is the development of Data Quality Objectives (DQOs). The DQO process, a systematic planning tool for establishing criteria for data quality and for developing data collection designs, assures that the type, quantity, and quality of environmental data used in decisionmaking will be appropriate for the intended application. DQOs are qualitative and quantitative statements that clarify the study objectives, define the most appropriate type of data to collect, determine the most appropriate conditions for data collection, and specify tolerable limits on decision errors. Performance requirements are established before the study begins by considering the consequences of decision errors and setting tolerable limits; and the data collection design is based on these criteria. Additional information on the DQO process may be found in EPA guidance (U.S. EPA, 1994).

Generally, quality assurance provides the user of data assurance that it meets defined standards of quality with a stated level of confidence (Taylor, 1987). Precision, accuracy, completeness, representativeness, comparability, and detection limits may be used as indicators of data quality. The DQO System provides the basis for linking the intended use of the data to the QA/QC requirements for data collection and analysis.

2.8.1 Quality Assurance

Quality assurance requirements may be found in the Good Laboratory Practice (GLP) Standards (U.S. EPA, 1989). These regulations "define the function of the quality assurance unit (QAU) in regulated studies as that of ensuring managers that all aspects of the facility, personnel, performance, record-keeping, and reporting are consistent and in compliance with the regulations. The objective of the regulations is to ensure users...of (the generated) information...of accuracy and to ensure integrity of study conduct and reported results according to specifications in the GLPs. This objective is achieved through the development of quality assurance programs that systematically evaluate and monitor...studies, as well as the activities of the facility and personnel."

Consideration of Good Laboratory Practices. The provisions of the Good Laboratory Practice Standards are intended to assure the quality and integrity of data submitted to the Agency (U.S. EPA, 1989). In conducting a study and submitting the data, the investigator must consider the provisions of the GLP standards. Some highlights of the GLP standards that are particularly applicable to postapplication exposure studies include:

- Test Substance Characterization (40 CFR 160.105). Test substances used in studies must be characterized according to the Good Laboratory Practices (GLPs) presented in 40 CFR 160. The investigator should characterize materials PRIOR to performing field trials. Aliquots of the test substance(s) should be retained during field trials for analysis, if any questions arise regarding the validity of the test substance(s). Test substance(s) include for the purposes of Series 875 Group B any materials containing the pesticide(s) of interest used in field trials or sample analysis.

- Protocol Requirements (40 CFR 160.120). The GLPs require that “each study shall have an approved written protocol that clearly indicates the objectives and all methods for the conduct of the study.” Each protocol should contain the following: a title and statement of purpose; identification of the test, control, and reference substances; names and addresses of the sponsor and performing laboratory; proposed experimental start and termination dates; justification for selection of test system; procedure for identification of the test system; a description of the experimental design; a description of the materials used to solubilize or suspend the test, control, or reference substances before mixing with the carrier; the route of administration and the reason for its choice; dosage level (i.e., application rates); sponsor approval dates and study director signature date; a statement of proposed statistical method; and signed protocol amendments.

- Sample Receipt, Handling, and Tracking (40 CFR 160.130). Critical to the success of any laboratory operation are the sample receipt, handling, and tracking procedures. Each sample must be identified with an individual code number. Sample receipt and storage inventories must also be maintained in accordance with the GLPs. Storage facilities must be maintained

at constant temperatures. Daily records must be collected to verify conditions. Sample shipments must be made using the most expeditious and appropriate method to ensure the integrity of the field samples. Laboratory operations should maintain Standard Operating Procedures (SOPs) for the operations described above.

- Sample Storage (40 CFR 160.41). As soon as samples reach the laboratory from the field, all samples held in ice chests must be stored in a refrigerator or freezer, as appropriate, pending further treatment. A sample history sheet should be prepared to document laboratory operations. A convenient sheet of this type contains columns labeled: sample number, date sample was collected, date of extraction, date of analysis, and the name(s) of the individual(s) responsible for the task. The lower portion of the sheet contains spaces for recording the conditions of storage for pads, other matrices, extracts, the extraction procedure employed, and the analytical procedure used.

In a study design expected deviations from GLPs need to be listed and discussed. GLP deviations should be presented concurrently with any protocol deviations along with their potential study impacts as required in the GLPs.

2.8.2 Quality Control

Appropriate quality control procedures are critical to the successful completion of any study conducted under these guidelines. Investigators are encouraged to refer to Part C - Quality Assurance/Quality Control for detailed guidance pertaining to the development of a study protocol, issues pertaining to field sampling procedures, and issues pertaining to residue chemistry.

2.9 CONTINGENCY PLANNING

The study design should include contingency plans for major weather events, attrition of study participants (e.g., due to heat exhaustion), or other circumstances that may adversely affect successful study completion.

2.10 REPORTING AND RECORD KEEPING

Study reports should contain the types of information described in this section as well as the justification for each aspect of the study. The interpretation of study results depends upon the understanding provided in the report concerning the study design (e.g., the rationale used for site selection and the identification of activities to be monitored are critical to interpreting the study). Data used in developing a technical approach and any decisions based on best professional judgment should be documented in study reports. Any *Confidential Business Information (CBI)* as stipulated under Section 106 of FIFRA should be

clearly noted and claimed as CBI as described in FIFRA submission instructions to the Agency (FIFRA, 1988).

REFERENCES FOR PART B, CHAPTER 2

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